

eolf-seql
SEQUENCE LISTING

<110> Sanofi

<120> Exendin-4 Derivatives as peptidic dual GLP-1/Glucagon Receptor Agonists

<130> DE2014/029

<150> EP14305501.0

<151> 2014-04-07

<160> 25

<170> PatentIn version 3.5

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<212> PRT

<213> Heloderma suspectum

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<222> (39)..(39)

<223> Amidated C-terminus

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His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu
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Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
			35			

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<213> Homo sapiens

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<222> (30)..(30)

<223> Amidated C-terminus

<400> 2

His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Val	Ser	Ser	Tyr	Leu	Glu	Gly
1				5					10					15	

Gln	Ala	Ala	Lys	Glu	Phe	Ile	Ala	Trp	Leu	Val	Lys	Gly	Arg
			20					25					30

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<212> PRT

<213> Homo sapiens

<400> 3

His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser
1				5					10					15	

Arg	Arg	Ala	Gln	Asp	Phe	Val	Gln	Trp	Leu	Met	Asn	Thr
			20					25				

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<222> (20)..(20)

<223> Lys is functionalized at the amino side chain group as
Lys((S)-4-carboxy-4-hexadecanoylamino-butryl)

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His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Val	Ser	Ser	Tyr	Leu	Glu	Gly
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eolf-seql

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Arg Gly Arg Gly
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<210> 5
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Tyr Ala Glu Gly Thr Phe Ile Ser Asp Tyr Ser Ile Ala Met Asp Lys
 1 5 10 15

Ile His Gln Gln Asp Phe Val Asn Trp Leu Leu Ala Gln Lys Gly Lys
 20 25 30

Lys Asn Asp Trp Lys His Asn Ile Thr Gln
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 <223> Xaa is Aib

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 <223> Lys is functionalized at the amino side chain group as
 Lys((S)-4-carboxy-4-octadecanoylamino-butryl)

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<223> Xaa is Aib

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<222> (29)..(29)

<223> Xaa is D-Ala

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<222> (39)..(39)

<223> Amidated C-terminus

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His	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Lys	Asp	Glu
1				5					10					15	

Gln	Arg	Ala	Lys	Leu	Phe	Ile	Glu	Trp	Leu	Xaa	Ala	Xaa	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
			35			

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<223> Xaa is Aib

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<223> Lys is functionalized at the amino side chain group as

Lys((S)-4-carboxy-4-((S)-4-carboxy-4-hexadecanoylamino-butyrylami
no)-butyryl)

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<223> Xaa is Aib

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<223> Xaa is D-Ala

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<222> (39)..(39)
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His	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Lys	Asp	Glu
1				5					10					15	

Gln	Arg	Ala	Lys	Leu	Phe	Ile	Glu	Trp	Leu	Xaa	Ala	Xaa	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
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Lys((S)-4-Carboxy-4-((S)-4-carboxy-4-hexadecanoylamino-butyrylami
no)-butyryl)

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<222> (27)..(27)

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His	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Lys	Asp	Glu
1				5					10					15	

Gln	Arg	Ala	Lys	Leu	Phe	Ile	Glu	Trp	Leu	Xaa	Ala	Gly	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
			35			

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Lys((S)-4-Carboxy-4-octadecanoylamino-butyryl)

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His	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Lys	Asp	Glu
1				5					10					15	

Gln	Arg	Ala	Lys	Leu	Phe	Ile	Glu	Trp	Leu	Xaa	Ala	Gly	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
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Lys((S)-4-carboxy-4-hexadecanoylamino-butryl)

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<223> Xaa is Aib

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<223> Amidated C-terminus

<400> 10

His	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Lys	Asp	Glu
1				5					10					15	

Gln	Arg	Ala	Lys	Leu	Phe	Ile	Glu	Trp	Leu	Xaa	Ala	Gly	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
			35			

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Lys((S)-4-carboxy-4-hexadecanoylamino-buteryl)

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His Xaa Gln Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Lys Asp Glu
1 5 10 15

Gln Arg Ala Lys Leu Phe Ile Glu Trp Leu Xaa Ala Xaa Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
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Lys((S)-4-Carboxy-4-((S)-4-carboxy-4-hexadecanoylamino-butyrylami
no)-butyryl)

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<222> (29)..(29)

<223> Xaa is D-Ala

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<222> (39)..(39)

<223> Amidated C-terminus

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His	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Lys	Asp	Glu
1				5					10					15	

Gln	Arg	Ala	Lys	Leu	Phe	Ile	Glu	Trp	Leu	Xaa	Ser	Xaa	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
			35			

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<223> Lys is functionalized at the amino side chain group as

Lys((S)-4-Carboxy-4-((S)-4-carboxy-4-hexadecanoylamino-butyrylami
no)-butyryl)

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His	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Lys	Asp	Glu
1				5					10					15	

Gln	Arg	Ala	Lys	Leu	Phe	Ile	Glu	Trp	Leu	Xaa	Ser	Gly	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
			35			

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<223> Lys is functionalized at the amino side chain group as

Lys((S)-4-Carboxy-4-((S)-4-carboxy-4-hexadecanoylamino-butyrylami
no)-butyryl)

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His	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Lys	Asp	Glu
1				5					10					15	

Gln	Arg	Ala	Lys	Leu	Phe	Ile	Glu	Trp	Leu	Xaa	Lys	Xaa	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
			35			

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 <223> Lys is functionalized at the amino side chain group as

Lys((S)-4-carboxy-4-((S)-4-carboxy-4-hexadecanoylamino-butyrylami
 no)-butyryl)

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His	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Lys	Asp	Glu
1				5					10					15	

Gln	Arg	Ala	Lys	Leu	Phe	Ile	Glu	Trp	Leu	Xaa	Lys	Gly	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
			35			

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<223> Xaa is Aib

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<223> Lys is functionalized at the amino side chain group as

Lys((2-{2-[2-(2-{2-[(4S)-4-Carboxy-4-hexadecanoylamino-butyrylami
no]-ethoxy}-ethoxy)-acetylamino]-ethoxy}-ethoxy)-acetyl)

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<223> Xaa is Aib

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<222> (39)..(39)
<223> Amidated C-terminus

<400> 16

His Xaa Gln Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Lys Asp Glu
1 5 10 15

Gln Arg Ala Lys Leu Phe Ile Glu Trp Leu Xaa Ala Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

<210> 17
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<223> Xaa is Aib

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<223> Lys is functionalized at the amino side chain group as

Lys((2-{2-[2-(2-{2-[(4S)-4-Carboxy-4-octadecanoylamino-butyrylami
no]-ethoxy}-ethoxy)-acetylamino]-ethoxy}-ethoxy)-acetyl)

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eolf-seql

<223> Xaa is Aib

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<222> (39)..(39)

<223> Amidated C-terminus

<400> 17

His	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Lys	Asp	Glu
1				5					10					15	

Gln	Arg	Ala	Lys	Leu	Phe	Ile	Glu	Trp	Leu	Xaa	Ala	Gly	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
			35			

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<222> (14)..(14)

<223> Lys is functionalized at the amino side chain group as

Lys([2-(2-{2-[2-(2-{2-[2-(2-Octadecanoylamino-ethoxy)-ethoxy]-acetylamino}-ethoxy)-ethoxy]-acetylamino}-ethoxy)-ethoxy]-acetyl)

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<223> Xaa is Aib

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<400> 18

His Xaa Gln Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Lys Asp Glu
1 5 10 15

Gln Arg Ala Lys Leu Phe Ile Glu Trp Leu Xaa Ala Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

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<223> Lys is functionalized at the amino side chain group as

Lys((2-{2-[2-(2-{2-[(4S)-4-Carboxy-4-(17-carboxy-heptadecanoyl)amino-butrylamino]-ethoxy}-ethoxy)-acetylamino]-ethoxy}-ethoxy)-acetyl)

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<400> 19

His	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Lys	Asp	Glu
1				5					10					15	

Gln	Arg	Ala	Lys	Leu	Phe	Ile	Glu	Trp	Leu	Xaa	Ala	Gly	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
			35			

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 <223> Amidated C-terminus

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His Xaa Gln Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Lys Asp Glu
1 5 10 15

Gln Arg Ala Lys Leu Phe Ile Glu Trp Leu Xaa Ala Xaa Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

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Lys((S)-4-Carboxy-4-((S)-4-carboxy-4-hexadecanoylamino-butyrylami
no)-butyryl)

<220>
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<223> Amidated C-terminus

<400> 21

His Xaa Gln Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Lys Asp Glu
1 5 10 15

Gln Arg Ala Lys Leu Phe Ile Glu Trp Leu Lys Ala Gly Gly Pro Ser
20 25 30

eolf-seql

Ser Gly Ala Pro Pro Pro Ser
35

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no)-butyryl)

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<400> 22

His Xaa Gln Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Lys Asp Glu
1 5 10 15

Gln Arg Ala Lys Leu Phe Ile Glu Trp Leu Lys Ala Xaa Gly Pro Ser
20 25 30

eolf-seql

Ser Gly Ala Pro Pro Pro Ser
35

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<400> 23

His Xaa Gln Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Lys Asp Glu
1 5 10 15

Gln Arg Ala Lys Leu Phe Ile Glu Trp Leu Xaa Ala Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
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<223> Amidated C-terminus

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His	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Asp	Glu
1				5					10					15	

Gln	Arg	Ala	Lys	Leu	Phe	Ile	Glu	Trp	Leu	Xaa	Ala	Gly	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
			35			

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eolf-seql

<222> (39)..(39)

<223> Amidated C-terminus

<400> 25

His	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Asp	Glu
1				5					10					15	

Gln	Arg	Ala	Lys	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Ala	Gly	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
			35			